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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/506,988	02/18/2000	Jordan J. N. Tang	OMRF 176	9126

7590

12/17/2001

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EXAMINER

SEAMAN, D MARGARET M

ART UNIT

PAPER NUMBER

1625

DATE MAILED: 12/17/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/506,988

Applicant(s)

TANG ET AL.

Examiner

D. Margaret Seaman

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-10 and 12 is/are rejected.
- 7) ☒ Claim(s) 5 and 11 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☒ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

DETAILED ACTION

1. In view of the Appeal Brief filed on 4 October 2001, paper #21, PROSECUTION IS HEREBY REOPENED. New grounds of rejections are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-4, 6-10 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are ambiguous due to the definition of "transition-state isostere". It appears that the transition-state isostere needs only two carbons in a tetrahedral conformation (see page 3 line 26). However, this appears to encompass many compounds including diols. Clarification is requested.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-4, 6-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention

based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims: The claims appear to encompass all compounds having two or more of two carbons in tetrahedral conformation.

The nature of the invention: The nature of the invention is aspartic acid protease inhibitors that are used to treat patients in need thereof.

The state of the prior art: The prior art has several compounds such as saquinavir, indinavir and ritonavir that have single transition-state isostere.

The level of predictability in the art: The level of predictability in the art is hard to describe when there is only one compound presented in the instant application that has two or more transition-state isosteres, namely compound identified as UIC-98-056.

The amount of direction provided by the inventor: There is little direction provided by the inventor due to the ambiguousness of the definition of "transition-state isostere" presented on page 3 line 26 of the instant application. The only working example is the one compound UIC-98-056. No other examples are given and no direction is provided by the inventor in the instant application as to what would be the next direction to go in which to seek other active compounds.

The existence of working examples: There is only one working example of a two transition-state isostere, UIC-98-056. The only example of a transition-state isostere is "-CH(OH)-CH₂-".

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The quantity of experimentation needed to make the instant invention is undue due to the lack of direction provided by applicants.

Taking the above factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make or use the instant invention, other than the one compound, identified as UIC-98-056.

6. Claims 1-4, 6-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It is not seen where the instant specification describes the instant invention such that the ordinary artisan could make or use the instant invention.

Specifically, the only description of a "transition-state isostere" in the specification is on page 3 line 26. A transition-state isostere is a compound wherein two carbon atoms in tetrahedral conformation mimic the transition state of catalysis. The only example of such two carbon atoms is "-CH(OH)-CH₂-". This is an ethyl alcohol. The specification shows only one compound, identified as UIC-98-056, having two such transition-state isosteres. There are no other examples of other carbon atoms in tetrahedral conformation that fit this definition. The specification fails to provide description for the scope of different compounds to be incorporated into the large and

structurally diverse compounds that potentially might fit this definition. The size, shape, and conformation which is dependent upon the therapeutic agent is considered critical to the practice of the presently claimed compounds/methods since such parameters have been demonstrated to be critical for obtaining efficacy (e.g. drug delivery). See *Ex Parte Bhide* (Bd Pat. App. & Int.) 42 USPQ2d 1441 (e.g. critical core structure necessary for biological activity must be present in the claimed invention). The prior art clearly demonstrates the criticality of the choice of compound, the amount or compound and the conditions (e.g. pH, temperature, administration time in order to achieve effective inhibition of protease) to incorporate compounds that are large in size and/or which differ in physical/chemical properties. This criticality results from the unpredictability of the compound in binding to the protease, which differs from compound to compound, and which are stereospecific with respect to the compound. Due to this, it is not seen where the instant specification adequately describes the instant invention.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Takatori (JP 09208450, CA 127:238926), Sugiura (CA 127:210184), and Kono (JP 09143044, CA 127:39539).

Takatori, Sugiura and Kono each disclose 1,3-butylene glycol which anticipates the instant claims. 1,3-butanediol (1,3-butylene glycol) fits the definition of having two transition-state isosteres. Two sets of two carbon atoms having tetrahedral conformation.

Claim Objections

9. Claims 5 and 11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. Margaret Seaman whose telephone number is 703-308-4528. The examiner can normally be reached on 630am-4pm, First Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat can be reached on 703-308-2439. The fax phone numbers

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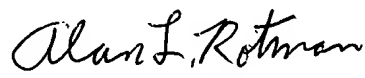
for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


D. Margaret Seaman
Primary Examiner
Art Unit 1625

dms
December 10, 2001


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PRIMARY EXAMINER